REMARKS

Claims 19-36 are pending. Claims 1-18 have been previously cancelled. Applicants acknowledge that the requirement for restriction has been deemed proper and is, therefore, made final. Accordingly, claims 24-33 are withdrawn from further consideration as being drawn to non-elected inventions. Claims 19-23 and 34-36 are currently under examination. Claims 19-23 and 34-36 are amended herein. New claim 37 is presented herein. Thus, amended claims 19-23 and 34-36 and new claim 37 are presently under consideration.

Support for the amendments to the claims is found throughout the specification and in the original claims. Specifically, support for amendment to claim 19 is presented in previously presented claim 19 and in the specification, for example, at page 11, lines 5-13 and at page 13, lines 6-9, wherein support for the phrase "sequences which have sufficient homology to hybridise thereto under medium stringency conditions, wherein washing is performed with 2 X SSC at 65°C" is found and at page 21, line 20 through to page 22, line 2 and Table 3, wherein support for the phrase "having an ability to modify tree height and/or internode length" is found. Claims 20-23 and 35 have been amended to replace the word "A" with "The" Claim 20 has been amended to reflect the election of a cucumber nucleic acid sequence for further prosecution. Claims 22 and 23 have been amended to clarify the subject matter of the claims. These claims are presently directed to a nucleic acid sequence in sense orientation, support for which is found at page 12, lines 14-20. Claims 35 and 36 are amended herein to clarify the method of the invention and to reflect the election of SEQ ID NO: 9 for continued consideration. Claim 36 is also amended herein to recite that the seed comprises the chimaeric gene, support for which is presented at page 11, lines 20-24. No issue of new matter is introduced by these amendments.

New claim 37 is presented herein. Support for new claim 37 is found at page 13, lines 12-13. No issue of new matter is introduced via this amendment.

Priority

The Examiner has acknowledged Applicants' claim for foreign priority based on an application filed in the United Kingdom on August 29, 1998. Accordingly, a certified copy of GB application number 9818808.9 is submitted herewith.

Specification

Claims 34 and 36 are amended herein to address objections raised with regard to improper form. Specifically, the claims have been amended to delete multiple dependencies referred to therein. Applicants believe that claims 34 and 36 as presently amended obviate this objection.

Information Disclosure Statement

The Examiner has indicated that four publications listed on form 1449 submitted on December 1, 2003 have not been considered as copies of these references were not provided by the Applicants. Accordingly, Applicants submit herewith legible copies of these references. Applicants apologize for the oversight that apparently led to the omission of these documents from an earlier submission.

Claim Objections

Claims 19, 20, 22, 34, and 36 are objected to for reading on non-elected inventions. In response, these claims have been amended such that they no longer read on non-elected inventions. Specifically, claim 19 has been amended to delete "in trees" therefrom. Claims 20-23 and 35 have been amended to recite "The" instead of "A" at the beginning of the dependent claims. Claims 22 and 23 have been amended to refer to "in sense orientation".

Rejections under 35 U.S.C. § 112

Claims 19-23 and 34-36 have been rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Specifically, claims 19 and dependent claims therefrom are allegedly indefinite for recitation of the terms "substantially similar" and "having the same function" in claim 19. Although Applicants assert these terms are sufficiently clear to a skilled practitioner in the art, claim 19 is amended herein to refer to "sequences which have sufficient homology to hybridise thereto under medium stringency conditions, wherein washing is performed with 2 X SSC at 65°C, said nucleic acid sequence encoding a polypeptide having an ability to modify tree height

and/or internode length ...". It should be noted that such hybridisation conditions are well known to an ordinarily skilled artisan and described in detail in numerous laboratory protocol references. Further, the replacement of the phrase "having the same function" in claim 19 with "encoding a polypeptide having an ability to modify tree height and/or internode length" renders apparent the function attributable to an expansin that establishes the metes and bounds of the claim. Applicants, therefore, believe that the amendments to claim 19 and dependent claims therefrom obviate the rejection of these claims under 35 U.S.C. §112, second paragraph.

Claims 19-23 and 34-36 have been rejected under 35 U.S.C. §112, first paragraph, for allegedly containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors were in possession of the claimed invention at the time the application was filed. The rejection appears to be directed to reference to sequences that are a "part thereof" of SEQ ID NO: 9 and sequences "substantially similar to SEQ ID NO: 9 and having the same function". In view of the amendment to the claim 19 and Applicants' arguments hereinbelow, the rejection, as it applied to claims 19-23 and 34-36, is respectfully traversed.

The present application reveals that expression of SEQ ID NO: 9 in a transformed tree is capable of modifying tree height and/or internode length in such transformed trees and thus a person skilled in the art would readily appreciate that homologous sequences, including parts of the sequence, may also possess expansin activity (i.e., have an ability to modify tree height and/or internode length in transformed tress) and, as such, are included with the scope of the present invention. Applicants assert that a person skilled in the art at the priority date of the present application would be able to determine which parts of an expansin sequence, such as SEQ ID NO: 9, encode a polypeptide capable of modifying tree height and/or internode length. Moreover, identification of sequences that are homologous to SEQ ID NO: 9 and encode polypeptides exhibiting the above-indicated expansin functions is also well within the capability of a skilled practitioner. The present specification presents nucleic acid sequences encoding seven expansin polypeptides (SEQ ID NOs: 1-6 and 9). These sequences amply describe sequences that fall within the scope of parts of SEQ ID NO: 9 and homologous sequences thereto. An ordinarily skilled practitioner would perform standard sequence analyses of SEQ ID

NOs: 1-6 and 9 to align the sequences and thereby, identify conserved amino acid residues and stretches of residues that constitute conserved sub-domains of these expansin polypeptides.

A skilled artisan would also be aware of the extensive literature pertaining to expansins that was available in advance of the priority date of the present application. Indeed, a number of references disclosing expansin sequences isolated from different species are cited in the present specification at page 7, lines 17-24 and were submitted for the Examiner's consideration in the IDS submitted on December 1, 2003. The Shcherban et al. reference (designated BG), for example, describes several expansin sequences isolated from a variety of organisms and provides an alignment analysis of the different expansin proteins. Applicants assert, therefore, that information readily available to the public in advance of the priority date of the present application, and particularly sequence alignments such as those presented in Shcherban et al., would facilitate identification of conserved regions of an expansin sequence (parts) and homologous sequences thereto.

Indeed, the Shcherban et al. reference presents guidance of particular utility for the design and identification of functional sub-domains or parts of an expansin polypeptide. As indicated by a sectional heading in this reference, which reads "Phylogenetically Conserved Sites Suggest Functional Regions", the authors have identified regions and amino acid residues of the expansin proteins that are highly conserved among a diverse range of species and correlated these structural elements of the expansins with functional properties. See page 9428, left column, second full paragraph. Shcherban et al. remark that "the N-terminal half of the expansin protein contains a series of 8 conserved cysteines with spacing similar to that of conserved cysteines in the chitin-binding domain of wheat germ agglutinin". Based on information relating to the structure of wheat germ agglutinin, the authors posit that the N-terminal half of the expansin protein may be folded and stabilized by disulfide bonds in a manner analogous to that of wheat germ agglutinin. Shcherban et al. also propose that the C-terminal one-third of an expansin protein, which comprises four tryptophans in a spatial organization reminiscent to that of the cellulose binding domains of cellulase, may also confer the ability to bind cellulose to expansins. Indeed, site directed mutagenesis was used to confirm the role of these tryptophan residues in cellulose binding. The authors also state that the presence of tryptophan and related amino acids

phenylalanine and tyrosine, which are known to facilitate binding to sugars in other proteins, indicates that the C-terminal half of expansin may be responsible for the ability of the polypeptide to bind to cellulose and related wall glycans.

A skilled practitioner in the field would, therefore, have been aware of the guidance offered by the Shcherban et al. reference with respect to delineation of structural/functional expansin sub-domains, and this information, in combination with expansin sequences presented in the specification and general knowledge pertaining to structure/function analyses performed on a vast array of proteins would have provided ample description regarding the choice of sub-domains/parts of an expansin polypeptide (e.g., SEQ ID NO: 9) which would be good candidates for functional assessment using the method of the invention.

Applicants also maintain that the identification of sequences which have sufficient homology to hybridise to SEQ ID NO: 9 under medium stringency conditions, wherein washing is performed with 2 X SSC at 65 °C, is well within the capabilities of an ordinarily skilled artisan. Such protocols are well known and described in numerous laboratory protocol handbooks that are readily available to molecular biologists. Moreover, searches of electronic databases that serve as repositories for entire genomic sequences can be performed with minimal effort and the parameters of such searches can be adjusted to mimic varying degrees of relatedness among sequences. In short, such electronically based searches can be customized to identify sequences of varying degrees of homology to a given sequence, such as SEQ ID NO: 9. Applicants, therefore, assert that presentation of expansin sequences SEQ ID NOs: 1-6 and 9 and the information publicly available at the priority date of the present application (e.g., the Shcherban et al. reference), in combination with the general knowledge and abilities of an ordinarily skilled practitioner, amply describe that which is meant by a part of SEQ ID NO: 9 or homologous sequence thereof possessing the claimed functional characteristics.

Claims 19-23 and 34-36 have been rejected under 35 USC § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one of skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In view of the amendments to the claims and Applicants' arguments hereinbelow, the rejection, as it applied to claims 19-23 and 34-36, is respectfully

traversed.

Claim 19, and dependent claims therefrom, have been amended to clarify the functionality which is shared among polypeptides encoded by SEQ ID NO: 9 and parts thereof and sequences which have sufficient homology to hybridise thereto under medium stringency conditions (wherein washing is performed with 2 X SSC at 65°C). As indicated herein above, the functionality relates to the capability of modifying tree height and/or internode length. Applicants assert that SEQ ID NO: 9 and sequences homologous thereto and parts thereof possessing these functional attributes are encompassed by the method of the invention. As described herein above, the conserved structure/function characteristics of the expansins were well known in the art at the priority date to which the present application is entitled. Indeed, the arguments set forth herein above are equally relevant in the context of the rejection of claims as allegedly not enabled by the specification.

Applicants assert that the level of skill in the art of biotechnology is high and thus obtaining parts of SEQ ID NO: 9 and/or homologous sequences thereto and assaying polypeptides encoded therefrom for function according to a detailed procedure as outlined in the present application does not constitute undue experimentation. Once such a sequence is chosen for further study, sub-domains or parts of SEQ ID NO: 9 can be generated readily by one skilled in the art by a variety of means, including polymerase chain reaction mediated amplification using primers designed to anneal at the terminal ends of the region to be amplified or restriction enzyme digestion of SEQ ID NO: 9, if such sites are conveniently arranged in the sequence. As described herein above, identification of sequences which have sufficient homology to hybridise to SEQ ID NO: 9 under medium stringency conditions, wherein washing is performed with 2 X SSC at 65 °C, is well within the capabilities of an ordinarily skilled artisan. Such protocols are a matter of common knowledge to ordinarily skilled practitioners and are described in detail in readily available laboratory protocol handbooks . Moreover, databases that serve as repositories for a plethora of sequences can be searched electronically with minimal effort, and the parameters of such searches can be refined to identify sequences possessing essentially any desirable degree of homology/identity. For the present application, for example, electronic database searches can be customized to identify sequences of varying degrees of

homology/identity to a given sequence, such as SEQ ID NO: 9. Such searches can, therefore, be used to identify sequences having sufficient homology to hybridise to SEQ ID NO: 9 under medium stringency conditions, wherein washing is performed with 2 X SSC at 65 °C. Applicants, therefore, assert that a skilled artisan who has read the present disclosure and is aware of the literature available at the priority date of the present application (e.g., the Shcherban et al. reference) would be able to practice the claimed invention by identifying a part of SEQ ID NO: 9 or a homologous sequence thereof and testing the sequence to determine if it exhibits the claimed functional characteristics.

Only routine experimentation would be required to determine the functionality of a polypeptide encoded by a part of SEQ ID NO: 9 or a sequence homologous thereto in a tree transformed according to the method of the present invention. The specification presents detailed methodology pertaining to transformation of trees and assessment of properties conferred by expression of genes transferred in the process. See, for instance, Example 3, at pages 18-20, wherein preparation of a transformation vector comprising an expansin sequence is described in step-wise fashion; and Example 4, at pages 20-22, wherein details pertaining to plant transformation and analysis of transformed plants are presented. Based on the guidance presented in the specification, personal experience, and general knowledge in the field, therefore, an ordinarily skilled artisan would understand how to design and make parts of SEQ ID NO: 9 and/or homologous sequences thereto and assay polypeptides encoded therefrom for function in accordance with the method of the present invention.

In response to the Examiner's comments pertaining to the Bowie et al. reference (1990, Science 247:1306-1310), Applicants maintain that the presentation of seven expansin sequences in the present specification (SEQ ID NOs: 1-6 and 9) and the availability of numerous expansin sequences via the published literature and accessible electronic databases serve to reduce uncertainty involved in determining which residues and/or regions of an expansin sequence may be important for protein function. Moreover, as reviewed herein above, the published literature also provides particular instruction with regard to residues and regions implicated in expansin function (e.g., the Shcherban et al. reference). Applicants, therefore, assert that the ample guidance presented in the specification and literature available before the priority filing date of

the application propels experimentation directed to expansin sequences and functional aspects associated therewith beyond many of pitfalls discussed in the Bowie et al. reference. Applicants also assert that the Bowie et al. reference, although relevant at the time of its publication (1990), is outdated and many experimental challenges described therein were likely rendered addressable by technological advances available at the priority date of the present application.

The Examiner's assertions pertaining to the McConnell et al. reference (2001, Nature 411:709-713) aside, Applicants contend that the state of the art relating to expansin sequences and polypeptides encoded therefrom and determinations of functionality ascribable thereto was highly evolved at the priority filing date of the present application. Moreover, the replacement of a glycine (a polar, but neutral amino acid) with either an alanine (non-polar amino acid) or an aspartic acid (anionic amino acid), as described in the McConnell et al. reference, would likely be anticipated to alter activity of a polypeptide. A skilled practitioner would certainly be aware of such considerations as they pertain to sequence design/choice in the present method.

The Examiner appears to have interpreted the Choi et al. reference (2003, The Plant Cell 15:1386-1398) as supportive of the contention that overexpressing expansins in plants can lead to unpredictable results. The Choi et al. reference is directed to an investigation of the *in vivo* functions of expansins in transgenic **rice** plants. Cultivated rice is generally considered a semiaquatic annual grass. Grasses are classified as monocots, which are characterized as angiosperms (flowering plants) having a single cotyledon (embryonic leaf) in the seed. Trees, which are the focus of the methods of the present invention, are generally classified as dicots (angiosperms having two cotyledons or embryonic leaves per seed) or gymnosperms (naked seed plants). It has been determined that angiosperms and gymnosperms diverged approximately 360 million years ago (Troitsky et al. 1991, J Mol Evol 32:253-261; see abstract attached hereto). Monocots and dicots are thought to have diverged approximately 200 million years ago, with an uncertainty of about 40 million years (Wolfe et al. 1989, Proc Natl Acad Sci USA 86:6201; see abstract attached hereto). The genetic relatedness of most trees and rice is, therefore, quite distant. Applicants assert that the findings of Choi et al., although informative with regard to expansin activity in transgenic **rice** plants, are not predictive of expansin activity in the vast majority of trees, which are dicotyledons or gymnosperms. Indeed, in view of the genetic distance evident between angiosperms and gymnosperms and between monocots and dicots, a skilled artisan would not view transgenic rice plants as a reasonable experimental model for

anticipating activity of any transgenic gene in a gymnosperm or dicot. Applicants, therefore, contend that the findings of the Choi et al. reference are neutral with regard to predicting the outcome of experiments wherein expansin expression levels are altered in transformed trees.

The Lee et al. (2003, Plant Physiology 131:985-997) reference is directed to overexpression of a soybean expansin in tobacco seedlings. Tobacco is classified in the Family Solanaceae or, more commonly, the night shade family. In addition to tobacco, the family includes eggplant, nightshade, paprika, chili pepper, tomato, potato, and petunia. In that members of the family can not reasonably be considered trees, Applicants assert that the findings described in this reference are not particularly germane to the presently claimed method which is directed to transformation of trees with sequences encoding expansins to modify tree height and/or internode length. As described herein above with regard to rice, the genetic distance between tobacco and trees is too great to support the use of tobacco as a model system in which to investigate and/or predict responses in trees. Accordingly, Applicants assert that the results described by Lee et al. are not predictive of results obtained using the present methods and, therefore, are not particularly pertinent to the claimed invention.

With regard to the Examiner's comments pertaining to undue experimentation, the law is quite clear. Applicants respectfully remind the Examiner that the courts have established a very high standard for what amounts to legally improper "undue experimentation".

1. *The legal standard for enablement imposed by 35 U.S.C. § 112, first paragraph.*

The first paragraph of Section 112 requires that a patent application be written so as to "enable any person skilled in the art to which it pertains...to make and use the same". Applicants through detailed objective guidance and examples teach the manner and process of making and using the invention in terms commensurate in scope with the claims. "Under these circumstances, the Specification is presumptively sufficient; it must be taken as ...[enabling] unless there is reason to doubt the objective truth of the statements contained therein which must be relied upon for enabling support". *In re Marzocchi & Horton*, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971) (emphasis in original); M.P.E.P. §706.03. It is well recognized that meeting one

stated objective is sufficient to satisfy the "how to use" requirement of Section 112.

2. *Some experimentation is specifically sanctioned.*

The law is clear that a Specification "may be enabling even though some experimentation is necessary", *United States v. Telectronics, Inc.*, 857 F.2d 778, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988) so long as the amount of experimentation required is not "undue experimentation". *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). The standard is whether or not the Specification "provides a reasonable amount of guidance with respect to the direction in which the experimentation should preceed". Id.

3. *No working examples are required.*

The law is also clear that no working examples are required in a Specification in order for it to meet the requirements of §112, first paragraph. *In re Borkowski et al.*, 422 F.2d 904, 164 USPQ 642 (C.C.P.A. 1970). The present Specification therefore goes far and beyond the requirement of the law.

4. *Analogous facts have led to a finding of enablement.*

A closer analysis of the relevant case law will also show that the present invention can be practiced as claimed without undue experimentation.

The Federal Circuit has specifically sanctioned a great deal of experimentation before the threshold into "undue experimentation" is crossed.

(a) In re Wands

The Federal Circuit considered what constitutes "undue experimentation" in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988) among other subsequent cases which have applied the principles set forth therein to other specific facts. In *Wands*, the Board of Patent

Appeals and Interferences had rejected a claimed immunoassay method for the detection of Hepatitis B virus using high-affinity monoclonal antibodies to a viral surface antigen (IgM anti-HBsAg antibodies) not enabled under §112, first paragraph. Evidence showed that over a two-year period some 140 hybridomas within the scope of the claims were produced, about 12 were tested, and about 5 of the 12 had the claimed affinity. The Federal Circuit articulated that a success rate of only 2.8% (representing 4 out of 143 hybridomas) would not necessarily have precluded legal enablement.

(b) Ex parte Mark

In *Ex parte Mark*, 12 USPW2d 1904 (BPAI 1989), Applicants claimed "A synthetic mutein of a biologically active native protein in which native protein has at least one cysteine residue that is free to form a disulfide link and is nonessential to said biological activity, said mutein having at least one said cysteine residues substituted by another amino acid and said mutein exhibiting the biological activity of said native protein". The Examiner found the claims to be non-enabling in that it would take undue experimentation to construct by recombinant methods (site-specific mutagenesis) all the muteins within the scope of the claims, and to screen the muteins produced for those which exhibit biological activity after modification. The Board of Patent Appeals and Interferences reversed the Examiner. The Board focused on the fact that Applicants could determine which are non-essential cysteine residues before doing mutagenesis. The Board noted that one skilled in the art could use the disclosed method and general knowledge of the art at the time the Application was filed to identify non-essential cysteine residues and substitute them for another amino acid within ten days.

In view of the proper legal standard set forth and exemplary case law interpreting the same, Applicants assert that the present Specification meets the requirements of the patent law regarding enablement. Based on general knowledge in the field and the teachings of the specification regarding methods for transforming trees with expansin sequences and assaying for phenotypic changes (such as modifying tree height and/or internode length) that result from expression of expansins encoded by these sequences, it would not require undue experimentation for a skilled artisan to perform experiments to determine if the presently claimed parts of SEQ ID

NO: 9 and homologous sequences thereto are capable of modifying tree height and/or internode length.

In view of the above, Applicants respectfully request that the Examiner reconsider the rejection of claims 19-23 and 34-36 under 35 USC § 112, first paragraph, as Applicants contend that the rejection is unduly restrictive.

Moreover, in view of the amendments to the claims and the arguments presented herein above, the Examiner is respectfully requested to reconsider and withdraw the rejection of the instant claims under 35 U.S.C. §112.

Rejection Under 35 U.S.C. § 102

The Examiner has rejected claims 19, 21-22, 34, and 36 under 35 U.S.C. §102(b) as allegedly anticipated by John et al. (January 1997, U.S. Patent No. 5,597,718). Applicants strenuously disagree with the Examiner's position with respect to an alleged relevance of U.S. Patent No. 5,597,718 (hereinafter referred to as the '718 patent). To begin, the Examiner's assertions aside, a person of skill in the art would not classify a cotton plant as a tree. The cotton plant belongs to the genus *Gossypium* of the family Malvaceae (mallow family). It is generally a shrubby plant having broad three-lobed leaves and seeds that are present in capsules, or bolls. The present invention relates to hardwood and softwood trees used in pulp manufacture. Cotton fiber ("seed hair") is a differentiated single epidermal cell derived from the ovule and is anatomically very different from wood fibers which are formed from cells in the xylen tissue of the stem. Further, the '718 patent does not refer to expansins and does not suggest a method of transformation involving an expansin capable of modifying tree height and/or internode length. Thus, Applicants maintain that the '718 patent does not anticipate the method of the present invention.

In order to underscore distinctive aspects of the invention, however, claim 19 is amended herein to clarify that the fiber characteristics modified by the present method pertain to tree height and/or internode length. In view of the arguments presented herein above and amendment to claim 19 and dependent claims therefrom, Applicants respectfully request that the rejection of claims 19, 21-22, 34, and 36 under 35 U.S.C. §102(b) be withdrawn.

Rejections under 35 U.S.C. §101

Claim 36 has been rejected under 35 U.S.C. §101 because the claim is allegedly directed to non-statutory subject matter. At the Examiner's suggestion, claim 36 has been amended to recite "seed comprising said chimaeric gene", thereby obviating the rejection.

Fees

No additional fees are believed to be necessitated by this amendment. However, should this be an error, authorization is hereby given to charge Deposit Account No. 11-1153 for any underpayment or to credit any overpayment.

Conclusion

It is submitted, therefore, that the claims are in condition for allowance. No new matter has been introduced. Allowance of all claims at an early date is solicited. In the event that there are any questions concerning this amendment, or application in general, the Examiner is respectfully urged to telephone the undersigned so that prosecution of this application may be expedited.

Respectfully submitted,

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Date: August 24, 2003

Enclosure: Petition for Three-Month Extension of Time
Copy of Information Disclosure Statement filed (IDS) on December 1, 2003 and Legible Copies of Four References (designated BC, BE, BH, and BK) Referred to Therein
Abstracts Only Wolfe et al. (1989, Proc Natl Acad Sci USA 86:6201) and Troitsky et al. (1991, J Mol Evol 32: 253)
Certified Copy of GB application number 9818808.9 and Transmittal Letter Thereto